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ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,694	AGNES ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER A. HIXSON	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40 and 42-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-57* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :5/12/2010, 5/12/2010, and 5/12/2010.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-40 and 42-57, drawn to methods for nucleating a solute in a solution which has a net charge.

Group II, claim(s) 41, drawn to a crystal formed by a method found in Group I.

2. The groups of inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The invention of Group II is directed to a crystal formed using the method of claim 1. Such a crystal might include, for example, a sodium chloride crystal, which is obviously well known in the art. Additionally, the methods of group I are known in the art, as shown below in the rejections under § 102. Accordingly, since the common technical feature linking these claimed groups is known, these groups suffer a lack of unity.

3. During a telephone conversation with Thomas Bailey on 7 July 2010 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-40 and 42-57. Affirmation of this election must be made by applicant in replying to this Office action. Claim 41 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Drawings

5. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because Figs. 2 and 3 are illegible. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

6. The abstract of the disclosure is objected to because it appears to exceed 150 words. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 1-4, 9-40, 42-44, and 46-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Regarding claims 1, 36, 42, and 46, each of these claims refer to a “primary vessel.” In the case of claim 36, the primary vessel refers to a “conduit holding [the] solution,” implying that in this claim (and its dependents), the vessel cannot be “wall-less.” In all other rejected claims, embodiments including "walled” and “wall-less” vessels are encompassed. However, the applicant, besides making a bald assertion that the vessel might be a capillary in [00074], does not provide sufficient detail regarding embodiments of walled vessels to convey that he had possession of that embodiment at the time of invention. Considerable detail was provided by the applicant,

however, in terms of wall-less vessels. Only a single example (p.42-45) was provided for an attempt at a walled vessel, however, the disclosed results do not convincingly convey that the walled vessel was effective at promoting crystal growth, since the objective measure of the S/N ratio was "not signifigantly different from that obtained" on a non-charged vessel. In particular, the number of protein crystals formed as measured in Figs. 13-14 are within the error of the experiments for charged vs. uncharged vessels. Droplets were described as being suitable containers for all embodiments, but the lack of specific effective guidance for walled vessels burdens one of ordinary skill in the art with the task of performing a burdensome exhaustive search to understand the details of practicing the method using anything other than the well described droplet.

Additionally, regarding claim 1, 22, 46, and 55, the applicant claims that his method is capable of being used on a molten metal or alloy droplet. However, the applicant, besides making a bald assertion that his method can be used for melts ([00027], does not provide even one more statement to indicate that he had possession of such an embodiment at the time of invention. Considerable detail was provided by the applicant, however, in terms of aqueous droplet containing solutes (p.23-end). Accordingly, this lack of specific guidance for practicing the method of metals, alloys, or melts, despite their unquestionable differences from the disclosed embodiments burdens one of ordinary skill in the art with the task of performing a burdensome exhaustive search to understand the details of practicing the method using anything other than the well described droplet.

Regarding claim 40, the limitation requires that the practitioner of the method “optimiz[e] the ionic make-up of [the] solution prior to applying the induction potential." The applicant's specification supports this step in paragraphs [00100]-[00104]. However, optimization can encompass a wide variety of steps not disclosed or even likely contemplated by the applicant. Accordingly, to fully practice this claim, one of ordinary skill in the art would be expected to undertake an exhaustive search to understand the complete range of optimizations available and useful to the method. The examiner believes that the applicant has failed to “convey with reasonable clarity to those skilled in the art that, as of the filing date sought, [he] was in possession of the

invention," since the invention is "for purposes of the 'written description' inquiry, whatever is now claimed," and a description of a single optimization is not sufficient to demonstrate that the full genus of all possible optimizations are in the possession of the applicant.

University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that "to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.* Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification must "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Accordingly, the above cited claims are rejected because the specification fails to convey with reasonable clarity to those skilled in the art the applicant was in possession of the claimed invention as of the instant applicant's filing date.

9. Claims 1-4, 9-40, 42-44, and 46-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for droplets as vessels, does not reasonably provide enablement for walled vessels. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ 1400 (CAFC 1988) at 1404 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation.

Attention is directed to In re Wands, 8 USPQ 1400 (CAFC 1988) at 1404 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation.

The nature of the invention In this case, the invention is directed to a method for promoting the crystallization of a solute dissolved in a solution contained in a vessel bearing a net charge. The claims refer to a "primary vessel." In the case of claims 36 and 37, the primary vessel refers to a "conduit holding [the] solution," implying that in this claim (and its dependents), the vessel cannot be "wall-less." In all other rejected claims, embodiments including "walled" and "wall-less" vessels are encompassed.

The state of the prior art Chung et al. (Journal of Crystal Growth 1998)(IDS)(Chung) indicates that "protein crystal experiments are difficult to control due to the large number of determining variables" (p.385, col. 1, first full paragraph). Bogan et al. (Journal of the American Society for Mass Spectrometry 2005)(IDS)(Bogan) teaches that a charged sample plate was ineffective at promoting the crystallization of a solute, since it did not perform better than an uncharged sample plate (p.260, col. 2 - 261 top of first column, and Fig. 6b and caption). Note that Bogan is a disclosure of the applicant himself.

The relative skill of those in the art Practitioners of this art are expected to have advanced degrees in science and/or engineering.

The predictability of the art As described by Chung, the art is unpredictable. This is true, since a wide variety of factors affect the crystallization of something as complicated as a protein.

The breadth of the claims The rejected claims generally broadly lay claim to crystallization of a solute after the walls of a walled vessel are subjected to an induction potential capable of providing a net charge to the walls of the container. The nature of

the container can generally be read to mean either a "wall-less" container (ie, a droplet) or a walled container.

The amount of guidance/working examples There is little more than an assertion that the vessel can have walls. No specific guidance either in the form of a specific description or a working example is provided, except that on p.42-45, a single example is provided, in which the applicants admit that the results are not within the range of error provided. The exact experiment disclosed in the specification was described as being unsuccessful in a publication by the applicants (see Bogan above in prior art section).

Quantitation of undue experiment Accordingly, in view of all of the preceding factors, since the applicants have not demonstrated how to perform the claimed method using a walled container, and in a publication, have actually indicated that use of a walled container would be unworkable, the amount of experimentation required of a practitioner of the method would certainly be undue, at least in regards to the full scope of the claimed subject matter and for claims 36 and 37, their full scope is not enabled.

All dependent rejected claims are rejected on the basis of their parent claim.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-40 and 42-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1, 42, and 46, the phrase “acquires a net charge” (claim 1, line 5) could be read to mean that the droplet changed its charge from a charged state to a neutral state. For the purpose of the prior art rejections below, it will be assumed to mean that a neutral droplet will acquire a non-zero electric charge.

Regarding claim 2, the phrase “threshold value” is not limited by a range, and for the purpose of the prior art rejection below will be assumed to mean a real number greater than or equal to zero.

Regarding claim 8, the applicant has provided an exhaustive list of devices capable of operating effectively in his claimed method. However, the applicant has a duty to clearly define the metes and bounds of his claim such that one of ordinary skill in the art can be expected to understand the claimed invention in order to avoid infringement. The long recitation provided here unduly complicates this task, and therefore renders the claim indefinite.

Regarding claim 15, the phrase “volatile solvent” (claim 15, line 2) does not clearly limit the type of solvent, since a "volatile solvent" entirely depends on the conditions of the unspecified environment in which the solvent is found during the practice of the claim. For the purpose of the prior art rejection below, the phrase volatile solvent will be interpreted to mean any solvent having a non-zero vapor pressure at standard temperature and pressure (STP).

Regarding claim 16, the examiner believes that the word “herein” should be replaced by “wherein.”

Regarding claim 19, the phrase "used to promote crystallization" (claim 19, line 2) does not require that a manipulative step be performed, and does not clearly define how claim 19 differs from its parent because of this.

Regarding claim 20, 22, 39 and 49, the requirement that the first solute or additive is a melt or a solid entirely depends on the conditions of the unspecified environment in which the solute and solvent are found during the practice of the claim. For the purpose of the prior art rejection below, these descriptions of the state of the material will be interpreted at STP and otherwise general laboratory conditions.

Further regarding claims 23-26, it appears that the applicant require that these claims depend on claim 22. However, the examiner is unaware of a "melt" in the context of these claims, and the applicant's specification only seems to refer to a "melt" in reference to metals and alloys, not biomolecules and proteins. Accordingly, the examiner interprets these claims as depending from claim 21 instead.

Regarding claims 21, 28, 54, and 55, requiring that the first solute or second solute be an inorganic compound or an organic compound does not appear to actually meaningfully limit the claim (since this appears to claim all possible chemical

compounds). Accordingly, these solutes will be required, for the purpose of the prior art rejection below, to be chemical compounds.

Regarding claim 40, the applicants have recited the general limitation of "optimization," without providing any description regarding what such a step would entail. Accordingly, the applicant has failed to provide clear and definite notice of the true metes and bounds of his claim, which renders this claim indefinite.

Regarding claim 50, the claim refers to an "identifying step" which lacks antecedent basis in claim 46. For the purpose of the prior art rejection below, the claim will be assumed to depend from claim 48.

Regarding claim 55, the claim does not end in a period.

Regarding claim 57, the claim improperly ends in ".1."

All dependent claims rejected are (also) rejected on the basis of their parent.

The Applicants are respectfully referred to the following excerpt from MPEP:

"§2171 **Two Separate Requirements for Claims Under 35 U.S.C. 112, Second Paragraph:**

> The second paragraph of 35 U.S.C. 112 is directed to requirements for the claims: The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
>
> There are two separate requirements set forth in this paragraph:
>
> > (A) the claims must set forth the subject matter that applicants regard as their invention; and
> > (B) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.
>
> The first requirement is a subjective one because it is dependent on what the applicants for a patent regard as their invention. The second requirement is an objective one because it is not dependent on the views of applicant or any particular individual, but is evaluated in the context of whether the claim is definite - i.e., whether the scope of the claim is clear to a hypothetical person possessing the ordinary level of skill in the pertinent art.
>
> Although an essential purpose of the examination process is to determine whether or not the claims define an invention that is both novel and nonobvious over the prior art, another essential purpose of patent examination is to determine whether or not the claims are precise, clear, correct, and unambiguous. The uncertainties of claim scope should be removed, as much as possible, during the examination process.

> The inquiry during examination is patentability of the invention as applicant regards it. If the claims do not particularly point out and distinctly claim that which applicants regard as their invention, the appropriate action by the examiner is to reject the claims under 35 U.S.C. 112, second paragraph. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). If a rejection is based on 35 U.S.C. 112, second paragraph, the examiner should further explain whether the rejection is based on indefiniteness or on the failure to claim what applicants regard as their invention. *Ex parte Ionescu*, 222 USPQ 537, 539 Bd. App. 1984)"

Furthermore:

"§2172 **Subject Matter Which Applicants Regard as Their Invention:**

> If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. See *Morton Int 'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993)."

In the present case, the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, and therefore rejection of the claims under 35 USC 112, second paragraph, is appropriate.

12. Claims 1-4, 9-40, 42-44, and 46-57 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that these claims fail to correspond in scope with that which applicant(s) regard as the invention can be found in Bogan (Journal of the American Society for Mass Spectrometry 2005)(IDS)(Bogan). In that paper, applicant has stated that a charged plate is not more effective at promoting crystallization than an uncharged plate, and this statement indicates that the invention is different from what is defined in the claim(s) because the applicants on p.42-45 assert the opposite, and in claims 36 and 37 explicitly claim a method which would embody such promotion.

Each of the rejected claims, at least within part of their scope, depends on a "walled" primary vessel. Sufficient support for such vessels can *only* be found on pages 42-45 of the applicant's specification. This section describes a control-type experiment

where protein solution is deposited on a charged and uncharged plate and the relative number of protein crystals is measured to determine if there is an advantage to such a charged plate. There the applicants allege that the experiment described there "could be of use for crystal growth" ([000130]). However, in Bogan, the applicants state that the identical experiment "suggests that there is no detectable difference in the two preparations [ie, a charged plate vs. an uncharged plate] with respect to .... crystal abundance or surface area" (quotation taken from p.261, top of col. 1, however, relevant text can be found on p.260-261 and Fig. 6b and its caption). The peer reviewed publication therefore contradicts the applicant's submission to the Office. Each of these claims is therefore rejected (especially claims 36 and 37 which are *solely* directed to walled primary vessels) to the extent that they recite subject matter that the applicant has admitted is not what he invented, ie claims directed to walled vessels in his method.

Claim Rejections - 35 USC § 101

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7, 9, 10, 12-25, 27-35, 38-40 and 42-47, 49, 51-57 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter or wholly preempts all practical uses of a judicial exception.

Regarding independent claims 1, 40, and 46, the examiner begins his analysis (as laid out in the Memoranda to the Examining Corps dated 24 August 2009 and slightly amended 28 June 2010, see <http://www.uspto.gov/patents/law/exam/memoranda.jsp>) by deciding that the claims under consideration are directed to the "process" subject matter category. The examiner then must decide if these process claims wholly embrace a judicially recognized exception, or if they are directed to a particular practical application of a judicial exception. In the case of claim 1, the method recites steps of "providing a primary vessel" which can include a droplet of a liquid as indicated by the applicant in

his specification, "applying an induction potential to [the] primary vessel such that said solution acquires a net charge," and "causing ion-induced nucleation of at least some of the first solution in a condensed phase." The preamble requires that the method "controllably induc[e]" the nucleation. The examiner finds that this claim is entirely directed to a natural phenomenon.

Bazilevskaya et al. (Journal of Atmospheric and Solar-Terrestrial Physics 2000)(Bazilevskaya) teaches that in a thunderstorm a charge separation occurs, such that the tallest point of the thunderstorm is charged more positively than the lowest point (p.1583, "4.3 Cosmic ray effect on the global electric circuit" "...placing in the troposphere thunderstorm clouds each with the positive charge at the top and negative charge at the bottom ..."), which implies that the aerosol droplets from which the cloud is formed (the "primary vessel") generally have a non-zero net charge in a thunderstorm cloud. It is similarly known, according to Simoneit et al. (Aerosol Science and Technology 1989)(Simoneit), that organic tracers including organic acids are frequently found in atmospheric aerosol particles (abstract). Muller et al. (Atmospheric Environment 2008)(Muller) even indicates that protein material is a common component of atmospheric aerosols (p.8040, "3.1.2 TRYLIS and TYLIS"). Similarly, salts and other inorganic compounds are generally dissolved in atmospheric aerosols as well. Finally, Lee et al. (Science 2003)(Lee) teaches that the gas-phase ion generation, similar to that discussed by Bazilevskaya, is an important source of nucleating agents (p.1887, col. 1, first complete paragraph). In combination, these references make clear that the claimed method occurs naturally in the atmosphere of our planet. Even the preamble recitation that the method be controlled does not alter this analysis, since the process is a naturally controlled process subject to regulation by natural processes established by the sun and the atmosphere's interaction. Nothing in the claimed method requires human intervention for its practice.

Claim 42 differs from claim 1 in that instead of requiring to "caus[e] ion-induced nucleation of at least some of the first solution in a condensed phase," it requires to "selectively caus[e] ion-induced precipitation of at least one of [the] solutes in a condensed phase." The ion-induced precipitation is a natural consequence of the

nucleation step recited in claim 1. And selectivity is not well defined in the claim. A broad but reasonable interpretation of "selective" is that species of low concentration cannot participate in the precipitation, and so the selectivity regards the precipitation of relatively high concentration species versus low concentration species.

Claim 46 adds the step of "depositing crystals derived from said nucleation on a substrate." This occurs as the crystals fall from the atmosphere to the ground.

Claims 1, 42, and 46 likewise fail the machine or transformation test. No machine is recited at all. And while the claims do recite a transformation (ie, the "nucleation of at least some of said first solute," in claim 1, and related limitations in claims 42 and 46), these limitations are not directed to a *particular* transformation. For the purpose of the claim, the solute can be anything. Even if the applicant can show that the transformation is a *particular* transformation, though, the transformation step is solely post-solution activity. Once the induction potential is applied to the primary vessel, the step of causing ion-induced nucleation and/or precipitation will necessarily occur. In other words, the only step which *arguendo* (because it recites a transformation, though not a particular transformation) allows the claimed method to pass the M-or-T test is inevitable once the other steps are accomplished. Additionally, as noted in the analysis above, there is nothing in the claim which would indicate that the claimed process is not drawn to a judicial exception; to the contrary, the analysis points decisively in the opposite direction.

For these reasons, claims 1, 42, and 46 are not directed to statutory processes under § 101.

All dependent rejected claims fail to cure the deficiencies of their parent claims.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. **Claims 1-21, 23-25, 27-30, 40, and 42-49** are rejected under 35 U.S.C. 102(b) as being anticipated by Chung et al. (Journal of Crystal Growth 1998)(IDS)(Chung) as evidenced by Bakhoum et al. (Analytical Chemistry 2005)(IDS)(Bakhoum).

Regarding claims 1, 5, and 6, Chung teaches the details of his method which provides a primary vessel for containing a solution with a solute (p.387, "3. Drop levitation and rotation"). The primary vessel is in the form of a wall-less liquid droplet. He then applies an induction potential to the vessel to provide a net charge (p.387, "3. Drop levitation and rotation"). Finally, this causes the ion-induced nucleation of at least some of the solute while remaining in a condensed phase (p.389, last paragraph of first column).

Regarding claims 2, 3, and 17, it is an inherent teaching of Chung that the step of ion-induced nucleation includes maintaining the surface charge density of the vessel to be above a threshold value. Since Bakhoum teaches that in a charged droplet, "the net charge resides in the diffuse layer at the droplet air interface" (p.3190, col. 1), the surface charge density of the vessel is non-zero, which is a threshold value. Charging the droplet therefore adjusts the surface charge density. This means that the ions causing the nucleation are located in the outer layer of the vessel.

Regarding claim 4, it is an inherent teaching of Chung that the ions in the vessel in excess of the counterions induce the heterogeneous nucleation of the solute. Bakhoum teaches that excess ions acts as the nucleation site (p.3191-3192, "NaCl Nucleation and Growth in Levitated Droplets with Net Charge").

Regarding claim 7, Chung levitates the droplet after the application of the induction potential (p.387, col. 2, "The droplet is then charged by induction upon applying and holding a high voltage .... The charged drop is then ultrasonically levitated...").

Regarding claim 8, Chung levitates the droplet in an acoustic balance (p.387, "...ultrasonically levitated ...").

Regarding claim 9, Chung's method causes formation of one or more nuclei (p.389, last paragraph first column). His method also delivers the nuclei to a target location (p.394, col. 1).

Regarding claim 10, Chung's method delivers the nuclei to a substrate (p.394, col. 1, slide cover).

Regarding claim 11, Chung's method delivers to a target location which (eventually) is located at a position remote from the levitation device (p.394, col. 1, air-tight cell).

Regarding claim 12, Chung's method delivers at least a part of the solution containing the nuclei (p.394, col. 1, where the droplet was retrieved).

Regarding claim 13, Chung's method transfers the nuclei from a primary vessel to a secondary vessel (p.394, col. 1, air-tight container).

Regarding claim 14, Chung's method allows at least some of the nuclei to seed crystal growth in the secondary vessel (p.394, col. 1, where "hundreds of micro-crystals started forming sporadically over the next day...").

Regarding claim 15, Chung's solution contains a volatile solvent (p.391, "5. Protein crystal growth using HUEL: preliminary study", water). The solvent evaporates from the vessel which causes an increase in the concentration of the solutes (Fig. 4).

Regarding claim 16, Chung's method allows the solvent to evaporate to yield a residue comprising one or more nuclei (Fig. 4).

Regarding claim 18, Chung's method includes the use of a surface tension modification agent (p.392, "6. Growth of lysozyme and thaumatin in weak agrose solutions," agarose).

Regarding claim 19, Chung's method uses the nuclei to promote crystallization (Fig. 5).

Regarding claim 20, Chung's method makes crystals of lysozyme, which in crystal form is a solid (Fig. 5).

Regarding claim 21, Chung's solute, lysozyme (Fig. 5) is an organic molecule.

Regarding claim 23, Chung's solute, lysozyme (Fig. 5) is a biomolecule.

Regarding claim 24, Chung's solute, lysozyme (Fig. 5) is a protein.

Regarding claim 25, Chung's solute, lysozyme (Fig. 5) is a protein, and proteins are organic acids, since they have a C-terminal end, which is a carboxylate group, and likely have acidic side chains as well.

Regarding claim 27, in another of Chang's embodiments, the first solute is thaumatin and the second solute is DL-tartaric acid or the buffer (p.393, col. 2).

Regarding claim 28, Chang's first and second solutes are organic molecules (p.393, col. 2).

Regarding claim 29, Chang selectively precipitates thaumatin (Fig. 6b).

Regarding claim 30, Chang separates the first solute from the second by selectively causing crystallization of the first solute (Fig. 6b).

Regarding claim 40, Chang optimized the ionic make up of the solution before applying the induction potential (p.393, col. 2).

Regarding claims 42 and 43, Chung teaches the details of his method which provides a primary vessel for containing a solution with a solute (p.387, "3. Drop levitation and rotation"). The primary vessel is in the form of a wall-less liquid droplet. He then applies an induction potential to the vessel to provide a net charge (p.387, "3. Drop levitation and rotation") which adjusts the mass to charge ratio. Finally, this causes the ion-induced nucleation of at least some of the solute while remaining in a condensed phase (p.389, last paragraph of first column). This process results in selectively causing ion-induced precipitation of at least one of the solutes into the condensed phase (Fig. 6b).

Regarding claims 44 and 45, it is an inherent teaching of Chung that the step of ion-induced nucleation includes maintaining the surface charge density of the vessel to be above a threshold value. Since Bakhoum teaches that in a charged droplet, "the net charge resides in the diffuse layer at the droplet air interface" (p.3190, col. 1), the surface charge density of the vessel is non-zero, which is a threshold value. Charging the droplet therefore adjusts the surface charge density. This means that the ions causing the nucleation are located in the outer layer of the vessel, which in Chung's case, is a droplet.

Regarding claims 46 and 47, Chung teaches the details of his method which provides a primary vessel for containing a solution with a solute (p.387, "3. Drop levitation and rotation"). The primary vessel is in the form of a wall-less liquid droplet. He then applies an induction potential to the vessel to provide a net charge (p.387, "3. Drop levitation and rotation"). This causes the ion-induced nucleation of at least some of the solute while remaining in a condensed phase (p.389, last paragraph of first column). Eventually, the grown crystals are deposited on a substrate (p.394, col. 1, slide cover), a predetermined target location.

Regarding claim 48, the structure of the crystals deposited on the substrate was identified (Fig. 6b, where the crystal was identified as thaumatin).

Regarding claim 49, the crystals deposited on the substrate were (relatively) pure (Fig. 6b).

16. **Claims 1, 5-10, 22, 46, 51, and 55** are rejected under 35 U.S.C. 102(a) and 102(b) as being anticipated by Kelton et al. (Physical Review Letters 2003)(Kelton).

Kelton teaches the details of his method which provides a melt primary vessel for containing a solution with a solute (p.195504-2, alloy liquid, first paragraph, col. 1). The primary vessel is in the form of a levitated wall-less liquid droplet, levitated by an electrostatic balance (p.195504-2, first paragraph, col. 1). He then applies an induction potential to the vessel to provide a net charge (p.195504-2, positive charge imparted, first paragraph, col. 1). Finally, this causes the ion-induced nucleation of at least some of the solute while remaining in a condensed phase (p.195504-1, first complete paragraph, col. 2). Eventually, the droplet is allowed to settle to a substrate after removed from the balance's field (implicit).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. **Claims 26, 33, 34, 51, 52, 54, and 56** are rejected under 35 U.S.C. 103(a) as being unpatentable over Chung in view of Bogan et al. (Analytical Chemistry 2002)(IDS)(Bogan) and Medzihradszky et al. (Analytical Chemistry 2000)(Medzihradszky).

Regarding claim 26, Chung does not teach to nucleate CHCA or THAP.

Bogan teaches that levitated droplets containing a MALDI matrix components can be used to form solid particles of matrix and analyte for subsequent MALDI-TOF-MS analysis (p.496, col. 2, first complete paragraph).

Medzihradszky teaches that he used CHCA as a MALDI matrix (p.555, “Results and Discussion”).

It would have been obvious to one of ordinary skill in the art to have modified Chung's method to co-crystallize CHCA and his solute to prepare them for a subsequent analysis.

Regarding claims 33 and 34, Chung does not teach to nucleate CHCA or THAP, to co-crystallize two solutes, or that the second solute is a MALDI matrix.

Bogan teaches that levitated droplets containing a MALDI matrix components can be used to form solid particles of matrix and analyte for subsequent MALDI-TOF-MS analysis (p.496, col. 2, first complete paragraph).

Medzihradszky teaches that he used CHCA as a MALDI matrix (p.555, "Results and Discussion").

It would have been obvious to one of ordinary skill in the art to have modified Chung's method to co-crystallize CHCA and his solute to prepare them for a subsequent analysis.

Regarding claims 51, 52, 54, and 56, Chung does not teach to nucleate CHCA or THAP, to co-crystallize two solutes, or that the second solute is a MALDI matrix.

Bogan teaches that levitated droplets containing a mixture of inorganic and organic solutes and MALDI matrix components which can be used to form solid particles of matrix and biomolecule analytes for subsequent MALDI-TOF-MS analysis (p.496, col. 2, first complete paragraph).

Medzihradszky teaches that he used CHCA as a MALDI matrix (p.555, "Results and Discussion").

It would have been obvious to one of ordinary skill in the art to have modified Chung's method to co-crystallize CHCA and his solute to prepare them for a subsequent analysis.

21. **Claims 31, 32, and 53** are rejected under 35 U.S.C. 103(a) as being unpatentable over Chung in view of Bogan and Medzihradszky as applied to claims 26, 33, 34, 51, 52, 54, and 56 above, and further in view of Julian et al. (Journal of Physical Chemistry B 2002)(IDS)(Julian).

Regarding claims 31, 32, and 53, neither Chung, Bogan, nor Medzihradszky explicitly teach that the method can be used for a first solute which is a stereoisomer or an enantiomer.

Julian teaches that in electrospray ionization (closely related to the method of claim 1) L- and D-serine form nuclei capable of nucleating crystallization (p.1221, col. 2, second and third complete paragraphs).

It would have been obvious to one of ordinary skill in the art at the time of invention to have made the first solute a stereoisomer or an enantiomer since Julian teaches that serine can form crystallization nuclei.

22. **Claim 35** is rejected under 35 U.S.C. 103(a) as being unpatentable over Chung in view of Bogan in view of Zaccaro et al. (Crystal Growth and Design 2001)(IDS)(Zaccaro).

Regarding claim 35, Chung does not explicitly teach that the method can be used to selectively separate a polymorphic form of the solute.

Zaccaro teaches by passing intense pulses of laser light during crystallization, a polymorphic form of gylcine was obtained (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have passed a laser light through the sample at the time of crystallization in order to separate a polymorphic form of the solute.

23. **Claim 38** is rejected under 35 U.S.C. 103(a) as being unpatentable over Chung in view of Julian.

Regarding claim 38, Chung does not explicitly teach that the method can be used to cause the differential precipitation of two different solutes.

Julian teaches that in electrospray ionization (closely related to the method of claim 1) L- and D-serine form nuclei capable of nucleating crystallization (p.1221, col. 2, second and third complete paragraphs) to form separate crystals of the L- and D- forms.

It would have been obvious to one of ordinary skill in the art at the time of invention to have used the method to cause the differential precipitation of two different solutes.

24. **Claims 39 and 50** are rejected under 35 U.S.C. 103(a) as being unpatentable over Chung.

Regarding claim 39, Chung does not explicitly teach that he added a solid to his solution to further induce nucleation of his solute.

He does indicate, however, that this is a future direction of his research (p.395, col. 2, where he indicates that he will attempt to directly control the number and size distribution of growing crystals by using a seeding method through which small uniformly sized crystals are introduced into the levitated droplet).

It would have been obvious, then, to one of ordinary skill in the art at the time of invention to have modified Chung's method to add a solid to his solution to further induce nucleation of his solute, since he indicated that adding seed crystals to his levitated droplet was an avenue he was considering pursuing to improve the quality of the crystals produced by his method.

Regarding claim 50, Chung does not explicitly teach that his method automatically deposits and identifies the crystals.

However, to provide a mechanical or automatic means to replace manual activity, which accomplishes the same result, is within the ambit of a person of ordinary skill in the art. See *In re Venner*, 120 USPQ 192 (CCPA 1958) (see MPEP § 2144.04).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to have modified Chung's method to automate certain tasks, since it is within the ambit of a person of ordinary skill in the art to replace manual activity with mechanical or automatic means.

25. **Claim 57** is rejected under 35 U.S.C. 103(a) as being unpatentable over Chung in view of rejected under 35 U.S.C. 103(a) as being unpatentable over Chung in view of

Bogan and Medzihradszky as applied to claims 26, 33, 34, 51, 52, 54, and 56 above, and further in view of Zaccaro.

Regarding claim 57, neither Chung, Bogan, nor Medzihradszky explicitly teach that the method can be used to selectively separate a polymorphic form of the solute.

Zaccaro teaches by passing intense pulses of laser light during crystallization, a polymorphic form of gylcine was obtained (abstract).

It would have been obvious to one of ordinary skill in the art at the time of invention to have passed a laser light through the sample at the time of crystallization in order to separate a polymorphic form of the solute.

Double Patenting

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

27. Claims 1-40 and 42-57 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 74 of copending Application No. 10/399823. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims at issue in the instant application and claim 74 of the conflicting application recite to provide a primary vessel for containing a solution (claim 74, (a) generating a discrete particle), applying an induction potential to the vessel so that it acquires a net charge ((b) inducing a net charge onto said discrete particle). The other steps are disclosed in the specification and later claims, and are therefore obviously considered by the applicant. The step of causing ion-induced nucleation is generally inevitable after the listed steps are completed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER A. HIXSON whose telephone number is (571)270-5027. The examiner can normally be reached on M-F 8 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

7/29/2010

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

cah